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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/425,956	10/25/99	TANZI	R 0609.4110001

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EXAMINER	
DUFFY,P	
ART UNIT	PAPER NUMBER
1645	8

DATE MAILED: 04/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/425,956	Tanzi et al.
	Examiner	Group Art Unit
	Duffy	1645

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 2-14-01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-34 is/are pending in the application.

Of the above claim(s) 31-34 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-30 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-34 are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

DETAILED ACTION

1. Applicants response of 2-14-01 has been entered into the record.

Information Disclosure Statement

2. Applicants have directed the examiners attention to a copending application 08/249,819 filed August 8, 1994 entitled that is directed to related technical subject material and requests that the cited application and the art therein to be considered during examination. This application and references therein are not available to the examiner since it is on appeal at the Board of Patent Appeals and Interferences. Applicant is advised that the date of any re-submission of any item of information contained in the information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Priority

3. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent

application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Drawings

4. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Election/Restriction

5. Applicant's election without traverse of Group I, claims 1-30 in Paper No. 7 is acknowledged.

6. Claims 31-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Double Patenting

7. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

8. Claims 17-30 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 17-30 respectively of prior U.S. Patent No. 5,972,634 this is a double patenting rejection.

9. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,972,634. Although the conflicting claims are not identical, they are not patentably distinct from each other because the term "antibody" of the patent is inclusive of both polyclonal and monoclonal antibodies. The use of a polyclonal antibody is obvious over the monoclonal antibody and vice versa.

Claim Rejections - 35 USC § 112

11. Claims 5-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompass methods which employ as a detection reagent polyclonal and monoclonal antibodies which specifically bind β1-40 but do not cross-react with β1-42 and polyclonal and monoclonal antibodies which specifically bind β1-42 but do not cross-react with β1-40. The specification fails to teach how to predictably and reproducibly make polyclonal and monoclonal antibodies with these specific binding properties. The specification fails to teach the appropriate immunogen and methods of making and screening for antibodies either monoclonal or polyclonal antibodies with the instantly claimed characteristics. Thus, one of skill would not know how to make the antibodies. As to polyclonal antibodies, the art specifically teaches that the production of polyclonal antiserum is variable and not readily reproducible. Campbell et al (page 3, column 2) teach that

> "Polyclonal antiserum consists of a wide variety of antibody molecules of different specificity and affinity (Fig. 1.1). Each time an animal is bled, it yields a different 'cocktail' of such antibodies as its immune response to the injected and environmental antigen alters and B cell clones emerge and recede. The same animal can yield a highly specific antiserum directed against the chosen antigen in one bleed and a poor antiserum in another . The animal also has a limited lifespan and prior to the days of Mab technology, the death of a single rabbit could cause major problems is a diagnostic laboratory.
>
> There is an additional inter-animal variability among animals which cannot readily be inbred in the same way as small rodents can be inbred to yield pure strains with matching histocompatibility antigens (Section 3.4). While large 'outbred' animals such a s rabbits, sheep and goats, can yield a large quantity of specific antibody, their response to antigen is variable and it was often necessary to immunise up to 30 animals to obtain a high-affinity antiserum."

Moreover, the specification fails to teach what immunogen would generate a polyclonal antibody with the instantly claimed properties. Because the peptides have identical sequences, immunization with the amyloid peptide (1-40 or 1-42) per se would generate a population of polyclonal antibodies which binds both because the skilled artisan would expect that antibodies

would be generated along the entire length of the peptide. Applicants have not taught how to make polyclonal antibodies with the instantly claimed specificity and thus the specification is not enabled for making and using polyclonal antibodies with these specific properties. Applicants have also not taught how to make and screen for monoclonal antibodies with the instantly claimed binding patterns. Consequently, in view of the utter lack of written description of how to make polyclonal antibodies and monoclonal antibodies with the instant binding specificity, and the lack of reproducibility of polyclonal antibodies the skilled artisan would have to develop specific immunogens and invent specific screening assays in order to identify antibodies with the instantly claimed characteristics and thus the skilled artisan would be forced into undue experimentation to make the instantly claimed polyclonal and monoclonal antibodies for use in the assay of the invention.

Applicants have previously argued this rejection in the prosecution of the parent application and such arguments have been carefully considered but are not persuasive for the reasons set forth below. Applicants' argue that it is well established that enablement is not precluded by some experimentation such as routine screening and cites *Hybridetch Inc. v. Monoclonal Antibodies, Inc.* 231 USPQ 81, 94 (Fed. Cir. 1986). This is not persuasive because as stated in the previous office action, mere screening is not that which is required for the production of polyclonal antibodies, the specification lacks immunogens of Mak et al for production, assays for screening and that the courts have held that "... whenever there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that

must supply the novel aspects of the invention in order to constitute adequate enablement." *Genetech Inc. v. Novo Nordisk A/S* 42USPQ2d 1001. The immunogens of Mak et al are not in the prior art. This knowledge of a specific starting material is not in the prior art. In addition, it does not obviate the rejection as it applied to predicable and reproducible generation of said polyclonal antibodies as taught by the Campbell reference of record. Thus, Mak et al, which fails to place the starting materials in the prior art (prior to the instant filing date) is not persuasive. Even though the methods of making antibodies are routine, in the instant case the starting materials (immunogens), nor the appropriate screening methods are provided for in the specification or the prior art. Thus, more than mere screening is required. Applicants' reliance on Iwatsubo et al is not persuasive because the claims are not limited to monoclonal antibodies. Applicants reliance on the letter from Dr. Cole is not persuasive because this private communication does not place the immunogen nor the methodology in the public domain at the time the invention was made. To arrive at the specific antibodies specific immunogens and mythological steps are suggested by Dr. Bush. Private communications fail to establish that the immunogen, process and products were well known in the prior art at the time the invention was made. That is the antibodies and methodology are not publicly available and do not establish that it was "*well known in the art*". In addition, "selectivity" of the antibody does not indicate that it does not cross react with the 1-42 as instantly claimed. Thus, does not support the claimed subject matter.

Citation and Discussion of Pertinent Prior Art

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

(a) Reynolds et al (U.S. Patent 4,504,585, March 12, 1985) teach an immunoassay format of --R + Ag (incubate) -----> (to form complex of) --R--Ag; --R--Ag + Ab* (incubate) to form ------> --R--Ag--Ab* wherein "R" is a nonimmunological, group specific ligand (column 3, see Detailed Description of the Invention). Reynolds et al teach that copper and zinc *chelates* are ligands useful for binding transferrin (column 4, fourth full paragraph) and that the primary capture antibody in a two site immunoassay may be substituted by a nonimmunological group specific ligand. Reynolds does not teach or fairly suggests heavy metal cations *per se* as a non-immunological binding partner would be useful in an immunoassay. Reynolds does not teach or fairly suggests blocking unbound metal ion sites and blocking unbound metal ions in an immunoassay.

(b) Voller et al teach heterogenous enzyme immunoassays wherein the binding of a secondary antibody is specifically detected by a labeled third antibody which binds the second antibody (see page 80, figure 2; Ab1-Ag-Ab2-anti-Ab2*). Voller et al teach conventional blocking methods to prevent non-specific binding of immunoassays but not for metal ions *per se*.

(c) Bush et al (Reference AS3) teach that Aβ binds the heavy metal cations zinc and copper, however the reference fails to teach or fairly suggest the use of heavy metal cations in an immunoassay for the detection and quantitation of Aβ-peptides.

Status of Claims

13. No claims are allowed.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
April 1, 2001

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600